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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/994,701	11/06/2001	Richard C. Willson	012MUS/96605	7906

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EXAMINER	
BURKHART, MICHAEL D	
ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/994,701	WILLSON ET AL.	
	Examiner	Art Unit	
	MICHAEL BURKHART	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2006; 7/3/2008; 10/24/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-13,16,22-25,29,30,32 and 34-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-13,16,22-25,29,30,32 and 34-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Claims 14, 15 and 31, corresponding to Group II in the restriction requirement dated 5/22/2008, have been canceled.

Applicants election of the species of RNA and IDA in the response dated 10/24/2008 is acknowledged. However, in light of the teachings of the prior art as set forth below, the species requirement of a specific ligand as recited, for example, in claim 44 is withdrawn, as is the species requirement for a type of target compound.

Claims 10-13, 16, 22-25, 29, 30, 32, 34-44 are pending and under examination.

Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: amended claims 10, 12, 23, and 36 recite the terms "DNA and/or RNA target compounds" or " DNA and/or RNA compounds", terms not found in the specification.

Claim Objections

Claim 23 is objected to because of the following informalities: "nucleic aid" in line 10 should be "nucleic acid." Appropriate correction is required.

Claim 40 is objected to because of the following informalities: "complex in performed in batch mode" in line 3 should be " complex is performed in batch mode." Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection necessitated by amendment of the claims in the response dated 10/27/2006.**

Claim 11 recites the limitation "the supernatant liquid" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 22-25, 29, 30, 32, 35, 36, 41 and 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Petty (Curr. Protocols Mol. Biol., 1996, of record). **This rejection is maintained for reasons made of record in the Office Action dated 2/8/2005, 6/27/2006, and for reasons set forth below. Claims 29, 30 and 32 have been added to the rejection due to amendment**

of the claims to be either properly dependent, or to be clear and concise under the provisions of 35 USC 112 2nd paragraph. Claims 41, 42 and 44 are new.

Regarding new claims 41 and 42, bacterial RNA and eukaryotic RNA comprise more than four non-shielded purines and pyrimidines, absent evidence to the contrary, i.e. tRNAs, rRNAs and mRNAs, all present in the lysates of Petty et al, can all comprise ten, hundreds, or thousands of non-shielded purines and pyrimidines. As a limited example, the mRNA encoding the histidine fusion protein of Petty et al is at the very least 18 residues: it must comprise the six histidine codons as taught in Figure 10.11B.1. Bacterial and eukaryotic cell lysates also comprise double stranded DNA in their genomes, and in any transfected plasmids. Regarding claim 42, it is considered that this is an inherent feature of the metal affinity column or the cell lysates of Petty et al, particularly in light of the other art of record wherein metal affinity was used to purify nucleotides (e.g. Hubert) and in light of the rarity of any given species of mRNA in a cell lysate amongst all other potential contaminants and RNAs. For example, the mRNA encoding the histidine fusion protein will only be one of perhaps thousands of mRNA molecules in the lysate. See MPEP 2112 in general for a discussion of inherency. Regarding claim 44, NTA is taught by Petty et al on page 10.11.10, first ¶.

Response to Arguments

Applicant's arguments filed 10/27/2006 have been fully considered but they are not persuasive. Applicants essentially assert that: 1) Petty is directed to protein purification, not nucleic acid purification; 2) Petty teaches adding protease inhibitors which is a step not required by the instant invention; 3) Petty teaches addition of DNAse, which would be disastrous in the instant invention; 4) Petty teaches purification only from *E. Coli*, whereas the instant invention

uses much broader sources; 5) Petty does not expressly or inherently teach treating lysates to recover DNA or RNA having at least four unshielded purines or pyrimidines; 6) Petty does not teach recovering DNA or RNA thus there can be no inherency; 7) Petty does not teach using mammalian cell lysates or patient cells as recited in the instant claims; 8) applicants favor a different metal (Cu) and chelator (IDA) than Petty; 9) Petty teaches a histidine fusion protein in his lysates, which is a contaminant in applicants view; 10) applicants favor ploy(a) mRNA which is not present in Petty's lysates; 11) Petty adds Mg and DNAse, rendering his methods useless for DNA purification; 12) Petty does not inhibit the activity of RNAse, which is important in many of applicants methods;

Regarding 1), 5), and 6), at the very least RNA is present in the bacterial cell lysates of Petty and thus is anticipatory of the claims as amended. See the further explanation above. Petty uses the same protocols and reagents (e.g. Ni-NTA resin, cell lysates comprising RNA) as the instant invention and thus inherently anticipates the claims. See MPEP 2112 for a discussion of inherency. There are no amendments to the instant claims stating that DNA or RNA is collected, furthermore the limitation was found in original claim 12, and considered anticipated by the elution conditions taught by Petty (previous Office Action).

Regarding 2), 3) and 11), the claims are worded with open language, e.g. "A method…comprising.." and thus embrace additional method steps. The step of adding a DNAse I, even if it were to degrade all DNA in the lysate, would still leave RNA available to bind to the Ni-NTA resin. This step would be seen as desirable in the purification of RNA, i.e. it is an easy step to remove DNA contaminants. There are no instant claims limited to the purification of DNA.

Regarding 4), 7) and 10), Petty teaches eukaryotic cell lysates for reasons of record (page 12 of the Office Action dated 2/8/2005, page 10.11.22 of Petty). Such cells inherently have poly(A) mRNA.

Regarding 8), 9), and 12), In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., methods using only Cu and IDA; methods wherein a histidine fusion protein is not present; the use of RNAse) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). This is not a 103 rejection, hence there is no need to argue "teaching away from." Ni-NTA is embraced by and recited in the instant claims (e.g. claim 44).

Claims 10-13, 16, 32, 34, 36-40 and 42-44 are rejected under 35 U.S.C. 102(b) as anticipated by Verdine et al (WO 98/00435, of record) or, in the alternative, under 35 U.S.C. 103(a) as obvious over Verdine et al as evidenced by Min et al (Nuc. Acids Res., 1996, pages 3806-3810). **This is a new rejection necessitated by amendment of the claims to recite DNA or RNA compounds comprising at least "four non-shielded…moieties", and, in some instances, that the target compound is collected substantially free of protein. Claim 32 has been amended to be clear and concise under the provisions of 35 USC 112 2nd paragraph, rendering clear what compound is being recovered, and what is not.**

Verdine et al teach a method comprising introduction of a single-stranded region (non-shielded) of nucleic acid as an affinity handle into the desired nucleic acid, followed by capture

of the desired nucleic acid by a technique that is selective for the characteristics of the affinity handle (see page 10, lines 1-5; page 11, line 1 through page 12, line 4). Verdine et al introduced a single-stranded region of nucleic acid into a desired nucleic acid by way of using the single-stranded region of nucleic acid as a primer to PCR amplify a target nucleic acid, thus the starting mixture comprised an enzyme, i.e. a DNA polymerase used in PCR reactions (page 3807, last ¶ , first column, Min et al, a publication describing the methods of Verdine et al). One of the primers was tagged with six successive 6-histaminylpurine residues (see page 9, lines 20-22 and page 10, line 3, "H_6-tagged primer"). Verdine denatured the resulting PCR product in 6M guanidinium-HCl (page 11, lines 6-7), thus exposing the single-stranded affinity handle. The tagged strand of the PCR product was immobilized on Ni^{2+}-NTA resin (page 11, lines 6-7), allowing it to be separated from the other strand. Note that either the tagged on non-tagged strand of the PCR product may be considered the DNA target compound. Supernatant containing contaminants such as the DNA polymerase was removed and purified DNA bound to the IMAC column was eluted with imidazole (Example 3, page 11).

Regarding claims 40 and 43, Verdine teaches incubating IMAC ligand with the target compound in batch mode (page 11, first ¶).

Regarding claims 42 and 43, the DNA primers were used at a picomolar concentration absent evidence to the contrary (Min et al, page 3807, first column, last ¶).

Regarding claim 37 and 39, the DNA compounds could be detected in eluted fractions via a radioactive label (Examples 2 and 3, beginning on page 11 of Verdine et al).

Regarding claim 38, the aim of Verdine et al was to purify single strand DNAs from double stranded PCR product and template. See Examples 1-3.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHAEL BURKHART whose telephone number is (571)272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Burkhart/
Primary Examiner, Art Unit 1633